

Does aeroallergen sensitivity and allergic rhinitis in children cause milder COVID-19 infection?

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ABSTRACT

Background: There are conflicting data with regard to the impact of respiratory and allergic comorbidities on the course of novel coronavirus disease 2019 (COVID-19) in children.

Objective: This study aimed to investigate the relationship between allergic diseases and COVID-19 severity in pediatric patients.

Methods: Seventy-five pediatric patients with COVID-19 were classified according to clinical severity and evaluated in the allergy/immunology and pulmonology departments 1 to 3 months after the infection resolved. Blood was collected from the patients for a complete blood cell count and assessment of immunoglobulin and total immunoglobulin E (IgE) levels, and skin-prick tests and spirometry tests were performed.

Results: A total of 75 patients ages 5–18 years were evaluated. COVID-19 was asymptomatic/mild in 44 patients and moderate/severe/critical in 31 patients. Based on allergy evaluation, allergic rhinitis was diagnosed in 19 patients (25.3%), asthma in 10 patients (13%), and atopic dermatitis in 3 patients (4%). Aeroallergen sensitivity was detected in 26 patients (34.7%). COVID-19 infection was asymptomatic/mild in 15 patients with allergic rhinitis (78.9%) and in 21 with aeroallergen sensitivity (80.8%) ($p=0.038$ and $p=0.005$, respectively). There was no difference in severity between the patients with and without asthma ($p=0.550$). The median (interquartile range) total IgE level was significantly higher in the asymptomatic/mild group (71.8 [30.7–211.2]) ($p=0.015$). There were no differences in terms of spirometry parameters.

Conclusion: Aeroallergen sensitization and allergic rhinitis in children may be associated with a milder course of COVID-19. The knowledge that atopy is associated with less-severe COVID-19 outcomes in children may guide clinical risk classification.

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a new type of human coronavirus that appeared in December 2019, and the disease it causes was named novel coronavirus disease 2019 (COVID-19) by the World Health Organization.¹ People with asthma and other allergic diseases are generally more susceptible to respiratory viruses, e.g., rhinovirus, which often cause acute exacerbation of asthma.² Early in the pandemic, it was predicted that patients with chronic respiratory disease would have a

higher incidence of COVID-19 as well as higher associated mortality and morbidity than the healthy population.³ However, there has been a significant decline in pediatric asthma-related emergency admissions compared with before the pandemic, independent of health-care avoidance.⁴ There is limited evidence about which underlying medical conditions in children might increase the risk for severe illness. Current evidence suggests that children with a medical complexity; with genetic, neurologic, metabolic conditions; or with congenital heart disease might be at increased risk for severe illness from COVID-19.

Similar to adults, children with obesity, diabetes, asthma or chronic lung disease, sickle cell disease, or immunosuppression might also be at increased risk for severe illness from COVID-19.^{5–7} Moreover, there are few data on whether asthma is a risk factor for severe COVID-19 in children or whether having COVID-19 will adversely impact asthma control. In a recent systematic review, only two reports included information on asthma as a potential risk factor for COVID-19 infection in children, but there were no data on severity or mortality.⁸ Beken *et al.*⁹ showed that asthma and atopic diseases did not increase hospitalization in

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children but did not mention any classification or comparison related to COVID-19 severity and atopy. However, the largest studies conducted to date have been limited to determining case numbers by age group, and, therefore, it remains unclear whether childhood asthma and atopy are related to the severity of COVID-19. The aim of this study was to investigate the impact of asthma, allergic rhinitis, and aeroallergen sensitivity on the severity of COVID-19 infection in pediatric patients.

METHODS

This prospective, multicenter study was conducted with children aged 5–18 years treated for COVID-19 infection between March 25 and November 20, 2020 in two tertiary pediatric hospitals (University of Health Sciences, Ankara Training and Research Hospital and Hacettepe University Children's Hospital) in Ankara, Turkey.

Study Protocol

At initial admission, the patients were evaluated by a pediatric infectious disease specialist (BCY, PDO) in the designated COVID-19 area of the pediatric emergency department. The patients included in the study were classified according to COVID-19 severity by a pediatric infectious disease specialist (BCY, KA, PDO, YO). The patients were evaluated in the pediatric allergy/immunology and pediatric pulmonology departments 1 to 3 months after discharge or with a negative polymerase chain reaction (PCR) test for SARS-CoV-2. The patients' demographic data, symptoms, physical examination and laboratory findings, and imaging studies during COVID-19 infection and hospitalization status were obtained from hospital records. Patients with acute upper respiratory tract infection illness within 2 weeks before the study and with known neurodevelopmental diseases were excluded. The patients were grouped according to the presence of atopic disease as assessed by the allergist and the presence of atopy according to skin-prick tests (SPT). The study was approved by the research ethics committee as well as the Public Health Agency of the Turkish Ministry of Health. Informed consent was obtained from all subjects (both the children and their parents).

COVID-19 Infection Diagnosis and Severity Classification. According to our national COVID-19 guidelines issued by the Coronavirus Scientific Advisory Board in our country, suspected cases were accepted as confirmed in the presence of positive reverse transcriptase PCR or serum-specific antibodies for SARS-CoV-2 (Coronavirus Scientific Advisory).¹⁰ COVID-19 severity was classified based on the patients' clinical

Table 1 Severity classification of coronavirus disease 2019 infection

Severity	Criteria
Asymptomatic infection	No clinical and radiologic findings
Mild disease	Findings of acute upper respiratory tract infection without clinical or radiologic signs of pneumonia
Moderate disease	Symptoms of respiratory tract infection and pneumonia
Severe disease	Progressive respiratory disease with dyspnea and central cyanosis
Critical illness	The presence of acute respiratory distress syndrome or respiratory failure, shock, or organ dysfunction, including encephalopathy, myocardial injury, coagulation abnormalities, and acute kidney injury

characteristics and results of laboratory examinations and radiologic imaging as described by Dong *et al.*⁵ (Table 1). Patients who were asymptomatic/mild according to the COVID-19 severity classification were combined into group 1 and patients who were moderate/severe/critical were included in group 2.

Pulmonary Function Testing. Spirometry (Spirolab II, Rome, Italy) was performed by following the American Thoracic Society and European Respiratory Society guidelines¹¹ at a minimum of 1 month after complete recovery or with a negative PCR test result for SARS-CoV-2. Spirometry parameters included forced vital capacity, forced expiratory volume in the first second (FEV₁), FEV₁ to forced vital capacity ratio, forced expiratory flow at 25% to 75% of the vital capacity, and peak expiratory flow.

SPT. Atopy was evaluated by using a SPT with common allergens: (1) house-dust mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinea*, *Acaridae*); (2) cat and dog dander, cockroach, latex; (3) fungi (*Alternaria alternata*, *Cladosporium*, *Aspergillus*); and (4) pollens (composite mix, *Parietaria*, *Secale*, tree mix, *Olecea*, grass mix, *Fraxinus*, *Cupressus*, alder, ragweed, *Salsola*, *Plantago*, *Chenopodium*, *Populus nigra*, *Tillia × europea*, *Betula pendula*, *Platanus occidentalis*, *Salix nigra*, *Pinus silvestris*, *Cynodon*, *Phleum pratense*) (ALK, Abello, Madrid, Spain).

Assessment of Underlying Conditions. The diagnosis of asthma was based on respiratory symptoms typical of asthma, with documentation of variable airflow

limitation by pulmonary function tests (data obtained from the file at the time of asthma diagnosis; these patients had been diagnosed with asthma for at least 1 year).¹² Allergic rhinitis was diagnosed in patients with two or more nasal symptoms (*i.e.*, congestion, rhinorrhea, sneezing, and itching) that persisted for at least 1 hour a day for > 2 weeks, with aeroallergen sensitization noted on SPT or allergen-specific immunoglobulin E (IgE)¹³ (Patients had symptoms of allergic rhinitis for at least 1 year). The diagnosis of atopic dermatitis was made according to the Hanifin-Rajka criteria.¹⁴ The patient's medical reports were evaluated by the allergist (EV), and the underlying diseases were defined. Written informed consent was obtained from the patients and their parents before the tests.

Statistical Analyses

Statistical analyses were performed by using SPSS software version 20.0 (IBM Corp, Armonk, NY). Data distributions were investigated by using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk test). Descriptive analyses were presented as mean \pm standard deviation for normally distributed variables and as median (interquartile range) for non-normally distributed and ordinal variables. Categorical variables were summarized as numbers and percentages. The Pearson χ^2 test was used in 2×2 tables for comparing differences between categorical variables. In comparisons of two independent groups, an independent samples *t*-test was used for normally distributed variables and the Mann-Whitney *U* test was used for non-normally distributed and numerical variables. A *p* value of <0.05 was considered statistically significant.

RESULTS

A total of 75 patients ages 5 to 18 years (mean \pm standard deviation, 13 ± 3.87 years) were included in the study, of whom 42 (56%) were boys. The COVID-19 severity classification was asymptomatic in 12 patients (16%), mild in 32 (42.7%), moderate in 30 (40%), and severe/critical in only 1 patient (1.3%). Forty-four of the patients (58.7%) were in the asymptomatic/mild group (group 1) and 31 (41.3%) were in the moderate/severe/critical group (group 2) (Fig. 1). The median (interquartile range) interval between the patients' COVID-19 diagnosis and an allergic and immunologic evaluation was 1 month (1–3 months). The patients' symptoms at the time of diagnosis are shown in Table 2. Of the 42 patients who were hospitalized (56%), 1 patient received oxygen support and none required noninvasive or invasive ventilation. All the patients had positive SARS-CoV-2 PCR results. Of the 15 patients who underwent a computed tomography (CT) of the chest, 11 had findings consistent with

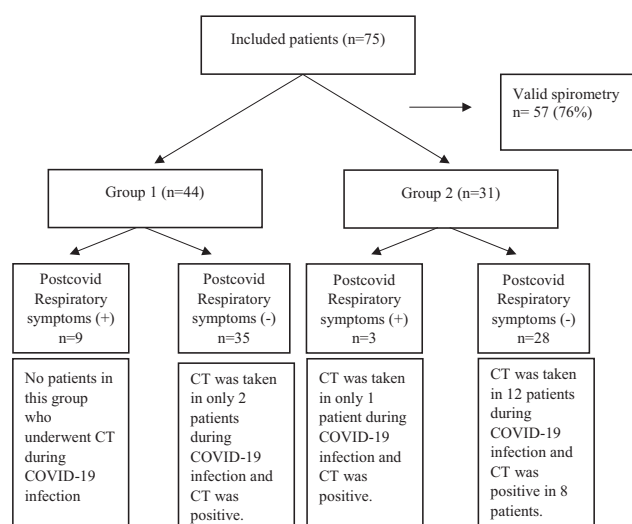


Figure 1. Post coronavirus disease 2019 (COVID-19) respiratory concerns and tomography results during infection according to the COVID-19 severity classification of the included patients.

COVID-19. Of these patients, 10 were hospitalized and 1 was followed up on an outpatient basis. Sixty-seven of the patients (91.8%) had a family history of COVID-19 infection.

Underlying Conditions

Thirty-two patients (42.7%) had an underlying disease. Of these, 12 (16%) had chronic pulmonary disease (10 of these had asthma) and 21 (28%) had allergic rhinitis or atopic dermatitis. Apart from these conditions, there was one patient each with neurologic disease, endocrine disease, metabolic disease, familial Mediterranean fever, and factor VIII deficiency (total of 5 patients).

Allergic Diseases

Based on an allergy evaluation, allergic rhinitis was diagnosed in 19 patients (25.3%), asthma in 10 patients (13%), and atopic dermatitis in 3 patients (4%). Aeroallergen sensitivity was detected in 26 patients (34.7%). The most commonly detected aeroallergens were grass mix and/or *Secale* ($n = 15$), house-dust mite ($n = 12$), cat or dog ($n = 6$), and *Alternaria* ($n = 2$). The comparison of allergic diseases according to COVID-19 severity is shown in Table 3.

Spirometry Results

All the patients included in the study underwent pulmonary function testing. There were no signs of upper respiratory tract infection in the patients at the time of pulmonary function testing. Fifty-seven of the patients (76%) were able to perform spirometry adequately for evaluation. These patients had similar clinical findings to the 18 patients whose spirometry results could not be evaluated. The nonreversible

Table 2 Clinical and laboratory findings in children with SARS-CoV-2 infection (N = 75)

Finding	Result
Asymptomatic, <i>n</i> (%)	12 (16)
Fever, <i>n</i> (%)	32 (42.7)
Respiratory symptoms, <i>n</i> (%)	
Cough	31 (41.3)
Respiratory distress	7 (9.3)
Gastrointestinal symptoms, <i>n</i> (%)	
Abdominal pain	8 (10.7)
Diarrhea	4 (5.4)
Nausea or vomiting	6 (8.1)
Influenza-like symptoms, <i>n</i> (%)	
Myalgia	27 (36)
Headache	20 (26.7)
Sore throat	14 (18.7)
Other, <i>n</i> (%)	
Loss of smell or taste	5 (6.7)
Laboratory evaluation	
Hemoglobin level, mean \pm SD, g/dL	13.4 \pm 1.6
Leukocyte count, mean \pm SD, cell/mm ³	6599 \pm 2198
Platelet count, mean \pm SD, cell/mm ³	260,561 \pm 2212
Neutrophil count, median (IQR), cell/mm ³	3000 (2000–4950)
Lymphocyte count, mean \pm SD, cell/mm ³	2045 \pm 1160
CRP, median (IQR), g/dL	0.92 (0.36–5)
Eosinophil count, mean \pm SD, cell/mm ³	93.2 \pm 77.6
Finding of CT of the chest consistent with COVID-19, <i>n</i> (%)	11 (14.7)

SARS-CoV-2 = Severe acute respiratory syndrome coronavirus 2; SD = standard deviation; IQR = interquartile range; CRP = C-reactive protein; CT = computed tomography; COVID-19 = coronavirus disease 2019.

obstructive pattern was observed in the pulmonary function tests of two patients, whereas one patient demonstrated a restrictive pattern. One of the two patients with an irreversible obstructive pattern on spirometry was diagnosed with Kartagener syndrome; the other patient had recurrent lung infection and was under follow up to determine the etiology, and had similar spirometry values to those before the COVID-19 infection. The patient with a restrictive pattern on spirometry was under follow up in the metabolism department due to biotin deficiency and did not have a spirometry evaluation before the COVID-19 infection. Spirometry results from all the patients with a valid spirometry are shown in Table 4.

Despite having recovered from COVID-19, 12 patients continued to have at least one pulmonary symptom (*e.g.*, cough, dyspnea, dyspnea on exertion) (Fig. 1). Of these patients with persistent symptoms, nine were evaluated at 1 month, one was evaluated at 2 months, and two were evaluated at 3 months after recovering from COVID-19. Two of these patients were follow-up patients with asthma whose asthma was well controlled before the COVID-19 infection. However, these patients were not using inhaled corticosteroid therapy as prescribed.

Another patient did not have a previous asthma diagnosis but had a history of recurrent asthma attacks and was diagnosed with asthma after demonstrating reversibility during assessment. There was no difference in this patient's respiratory symptoms before and after COVID-19 infection. Only this patient and the patient with a history of recurrent pulmonary infection and irreversible spirometry exhibited an obstructive pattern on spirometry; pulmonary function test results were normal in the other 10 patients. One patient had chronic pulmonary disease other than asthma, one patient had neurologic disease, and one patient had allergic rhinitis. Of the 12 patients with persistent respiratory symptoms after COVID-19 infection, 6 had no underlying disease and only 1 patient (with a history of recurrent lung infection) had CT imaging obtained during COVID-19 infection and the findings were evaluated as being consistent with COVID-19. A comparison of spirometry values according to COVID-19 severity is shown in Table 3.

DISCUSSION

In this study, children with aeroallergen sensitization and allergic rhinitis had milder COVID-19

Table 3 Comparison of allergic diseases and demographic characteristics according to COVID-19 severity classification*

Characteristic	Group 1: Asymptomatic/Mild	Group 2: Moderate/Severe/Critical)	<i>p</i>
Age, median (IQR), y	13.5 (8.1–16.3)	14.2 (11.4–16)	0.474
Sex, <i>n</i> (%)			0.265
Girls	17 (38.6)	16 (51.6)	
Boys	27 (61.3)	15 (48.3)	
BMI, median (IQR), kg/m ²	20 (15.9–23.5)	20.4 (6.8–23.1)	0.752
Asthma, <i>n</i> (%)	5 (11.4)	5 (16.1)	0.550
Ever wheezing, <i>n</i> (%)	12 (27.2)	14 (45.1)	0.109
Allergic rhinitis, <i>n</i> (%)	15 (34)	4 (12.9)	0.038[#]
Asthma and allergic rhinitis, <i>n</i> (%)	16 (36.3)	8 (25.8)	0.334
Atopic disease, <i>n</i> (%)	17 (38.6)	9 (29)	0.389
Aeroallergen sensitization, <i>n</i> (%)	21 (47.7)	5 (16.1)	0.005[#]
Parental allergy, <i>n</i> (%)	14 (31.8)	15 (48.3)	0.147
Passive tobacco smoke, <i>n</i> (%)	12 (27.2)	10 (32.2)	0.641
Prematurity, <i>n</i> (%)	3 (6.8)	3 (9.6)	0.687
Mode of delivery, <i>n</i> (%)			0.644
Cesarean	15 (34)	9 (29)	
Normal spontaneous vaginal delivery	29 (65.9)	22 (70.9)	
IgE level, median (IQR), IU/L	71.8 (30.7–211.2)	37.1 (18.9–72.9)	0.015[#]
Eosinophil count, median (IQR), /μL	145 (77.5–252.5)	150 (90–235)	0.779
IgG level, mean ± SD, mg/dl	1135 ± 206	1066 ± 229	0.191
IgA level, mean ± SD, mg/dl	138 ± 55	132 ± 58	0.7
IgM level, median (IQR), mg/dl	100.5 (77–138.2)	101 (79.7–144.5)	0.952
FVC % predicted, mean ± SD	104.7 ± 15.1	98.2 ± 9.4	0.103
FEV ₁ % predicted, mean ± SD	97.9 ± 15.1	90.6 ± 10.6	0.073
FEF _{25–75} % predicted, mean ± SD	101.4 ± 31.8	90.2 ± 25.2	0.199
FEV ₁ /FVC, median (IQR)	0.92 (0.86–0.94)	0.89 (0.83–0.96)	0.801

COVID-19 = Coronavirus disease 2019; IQR = interquartile range; BMI = body mass index; IgE = immunoglobulin E; SD = standard deviation; FVC = forced vital capacity; FEV₁ = forced expiratory volume in the first second; FEF_{25–75} = forced expiratory flow at 25% to 75% of the vital capacity.

*Categorical variables were compared by using the χ^2 test; numerical variables were compared by using the Mann-Whitney U test.

#Bold data are those with a *P* value < 0.05.

infection, whereas children with asthma showed no difference in terms of COVID-19 severity. In addition, total IgE values were higher in the group who

experienced milder COVID-19 infection. Although it is now well known that age, smoking history, and certain comorbidities (e.g., hypertension, diabetes, obesity, and coronary artery disease) are risk factors for severe COVID-19, the effect of asthma on COVID-19 severity is controversial.^{5,15} There are significantly fewer data with regard to COVID-19 symptoms and risk factors in children than in adults. However, children have a lower rate of mortality due to COVID-19 and are considered to be at lower risk of severe respiratory tract findings than adults.¹⁶ In a retrospective study of 177 children positive for COVID-19 and young adults, asthma was found to be the most common comorbid condition, with an overall prevalence of 20%.¹⁷ However, asthma was not more frequent among patients who were hospitalized or critically ill.¹⁷ Similarly, in a study of 46 patients, ranging from 1

Table 4 Spirometry results from all patients with a valid spirometry

FEV ₁ % predicted, mean ± SD	95.5 ± 14.1
FVC % predicted, mean ± SD	102.5 ± 13.8
PEF % predicted, mean ± SD	88.6 ± 14
FEF _{25–75} % predicted, mean ± SD	97.7 ± 30
FEV ₁ /FVC, median (IQR)	0.92 (0.85–0.95)

FEV₁ = Forced expiratory volume in the first second; SD = standard deviation; FVC = forced vital capacity; PEF = peak expiratory flow; FEF_{25–75} = forced expiratory flow at 25% to 75% of the vital capacity.

month to 21 years of age, who were hospitalized for COVID-19, asthma was present in 24.4% of the patients but was not associated with poorer outcomes or pediatric intensive care unit admission.¹⁸

Asthma and atopy are well-known risk factors for viral respiratory tract infections and are associated with worse outcomes than that seen in the healthy population.¹⁹ Patients with atopic asthma are more susceptible to severe clinical symptoms caused by rhinoviruses and respiratory syncytial virus.^{20,21} Cold viruses such as adenoviruses, enteroviruses, and seasonal coronaviruses are associated with increases in asthma exacerbations.²² Similarly, asthma was one of the most common risk factors for hospitalization and death during the 2009 H1N1 influenza pandemic.²³ Although current evidence suggests that asthma and atopy pose a risk for poorer outcomes in respiratory viral diseases, the newly identified pathogen SARS-CoV-2 deviates from this trend.

Angiotensin-converting enzyme 2 (ACE2) is the main host cell receptor for SARS-CoV-2 entry.²⁴ Jackson *et al.*²⁵ determined that ACE2 expression was lower in individuals with atopy. Decreases in ACE2 expression levels have been associated with allergic sensitivity, higher total IgE levels, and type 2 inflammatory cytokines.²⁶ IL-13, a major type 2 inflammatory cytokine, has been found to significantly reduce ACE2 expression in airway epithelial cells.²⁶ Our finding that patients with aeroallergen sensitization and allergic rhinitis had milder COVID-19 infection may be partially explained by the above findings. Total IgE levels were evaluated 1–3 months after COVID-19 infection. Therefore, it is not known whether COVID-19 infection has an effect on total IgE levels. There is a need for studies that compare the values before COVID-19 infection. However, because the allergic rhinitis symptoms of patients allergic rhinitis in our study were at least 1 year before COVID-19 infection, it can be speculated that atopy and total IgE elevation may cause a milder COVID-19 infection in children.

Similar to our results, Keswani *et al.*²⁷ showed that atopy was associated with less severe COVID-19, whereas this relationship was not seen in asthma. Chibba *et al.*²⁸ also found that the prevalence of allergic rhinitis was 11.6% among the patients with COVID-19 and that those with allergic rhinitis were less likely to be hospitalized. In a retrospective analysis of all patients positive for SARS-CoV-2 in a large adult and pediatric tertiary center over a 2-month period, it was reported that COVID-19 severity did not differ according to atopy status but that, when corrected for the presence of COPD, COVID-19 may be less severe in patients with atopy but without asthma.²⁹

Asthma is a highly heterogeneous chronic inflammatory obstructive lung disease. The role of asthma and its association with COVID-19 severity are more complex.³⁰ Nonallergic asthma was associated with

prolonged intubation time in an earlier study.³¹ In a cohort study conducted in Korea, it was reported that allergic rhinitis and asthma, especially nonallergic asthma, led to a higher risk of susceptibility to SARS-CoV-2 infection and more-severe clinical outcomes.³² Zhu *et al.*³³ analyzed data from UK Biobank in their population-based prospective cohort study and showed that, although the risk of severe COVID-19 was higher in patients with nonallergic asthma, this risk was not significantly increased in allergic asthma. In our study, the patients with allergic rhinitis were found to have milder COVID-19 infection, whereas there was no difference in severity in children with asthma compared with those children without asthma. Due to the small number of patients with asthma, we were unable to compare allergic and nonallergic asthma in terms of COVID-19 severity. In a cross-sectional, retrospective, observational study of children conducted by Rabha *et al.*,³⁴ asthma was shown to be associated with lower respiratory tract involvement and worse COVID-19 severity scores, unlike in our study. The fact that our study included children ages 5–18 years instead of ages 0–18 years and was conducted prospectively may be the reason that our results differed from theirs. In addition, as mentioned above, they may have obtained different results from our study due to differences in terms of asthma endotypes.

Beken *et al.*⁹ examined the relationship between asthma and COVID-19 in children and reported that asthma did not pose a risk for hospitalization. Recently, Floyd *et al.*³⁵ investigated the prevalence of asthma in hospitalized and non-hospitalized pediatric patients with COVID-19 and found that an asthma diagnosis was negatively associated with hospitalization due to COVID-19. In these studies, COVID-19 disease severity was not evaluated; instead, comparisons were made according to hospitalization criteria. Because, for a certain period, our national health policy mandated that all patients diagnosed with COVID-19 be hospitalized and followed up, even if asymptomatic, in this study, we used the COVID-19 disease severity classification instead of hospital admission criteria. In addition, because our patients who were positive for COVID-19 remained in the hospital until SARS-CoV-2 PCR results were negative, it was not considered appropriate to provide data on their length of hospital stay.

Although some studies reported that the prevalence of asthma was lower among adults with COVID-19 than in the general population,^{36–40} other studies reported it to be higher, and regional differences were observed.^{41–44} The prevalence of asthma among pediatric patients with COVID-19 is low. In a study that evaluated 182 pediatric patients hospitalized for COVID-19, 22.8% of the patients were reported to have allergic disease, most commonly allergic rhinitis, but

there was no difference between patients with allergies and patients without allergies in terms of clinical and immunologic findings or disease severity.⁴⁵ In our study, the prevalence of physician-diagnosed asthma was 13%. This rate is similar to the overall prevalence of asthma in children in our country.

Persistent abnormalities have been reported in patients with COVID-19 pneumonia, most typically ground-glass opacity in the CT of the chest obtained at discharge, and this may affect pulmonary function. However, few studies evaluated patients with COVID-19 and with pulmonary function testing after infection. Although, in reality, patients should be evaluated both before and after infection to fully understand the effect of COVID-19 on respiratory function, this is not feasible due to the impossibility of predicting who will have COVID-19 infection and when. However, in a retrospective study conducted in a pediatric pulmonary rehabilitation center for children with chronic lung disease, there was no difference between children who were allergic and children who were not allergic in terms of COVID-19 test positivity or symptomatology, asthma remained under control in all patients, and the mean FEV₁ value measured 1 month after COVID-19 infection did not differ from baseline.⁴⁶ In our study, spirometry parameters did not differ according to COVID-19 severity.

To our knowledge, our study was the first prospective study that compared COVID-19 severity in pediatric patients according to the presence of atopy and their pulmonary function test results. However, one of the limitations of the study was the low number of severe and critically ill patients. Although the centers included in this study are tertiary, patients who were critically ill did not come for follow-up during this study. This may have prevented us from finding a significant difference in pulmonary function test results between the groups. Pulmonary function tests were not performed in all patients in the same time period but were done between 1 and 3 months after COVID-19 infection. The reason we were unable to evaluate some of the patients with pulmonary function tests was a lack of cooperation, despite the patients ranging in age from 5 to 18 years. In addition, only a simple spirometric examination was performed in our study. Although we detected no significant differences in the patients' simple spirometric examinations, it may be useful to evaluate patients with more-advanced methods of measuring pulmonary function in prospective studies.

CONCLUSION

Aeroallergen sensitization and allergic rhinitis in children may be associated with a milder course in COVID-19. The knowledge that atopy is associated

with less-severe COVID-19 outcomes in children may guide clinical risk classification.

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